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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,171	11/18/2003	Brent R. Constantz	SKEL-008	5987

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EXAMINER	
ARNOLD, ERNST V	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,171	CONSTANTZ ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/4/05, 1/3/05, 2/27/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges receipt of application 10/717,171 filed on 11/18/2003. Claims 1-29 are pending and, accordingly, are presented for examination on the merits.

The Examiner suggests that the Applicant remove the final semi-colon in step (iii) of claim 26. It is not required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 10, 11, 13, 15-17, 21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al. (US 5,525,148).

Claim 1 is drawn to a method of producing a flowable composition that sets into a calcium phosphate containing product, said method comprising: combining: (a) a setting fluid; (b) dry reactants comprising a calcium source and a phosphate source; and (c) an osteoclastogenic agent; in a ratio sufficient to produce said flowable material.

The instant specification defines osteoclastogenic agent as an agent that induces osteoclastogenesis, i.e., causes differentiation of hematopoietic monocyte/macrophage precursors into osteoclasts.

Chow et al. disclose the preparation of calcium phosphate cements by combining a first component comprising a calcium source and a phosphate source (as a powder; hence dry) and a second component comprising an aqueous setting fluid (Column 8, lines 4-15). The resulting composition can be readily modeled to accurately reconstruct bony cavities and missing bone and can be molded and sculpted or even supplied as a putty (Column 4, lines 30-38 and column 11, lines 3-7). The Examiner interprets that the ease of manipulation of the composition of Chow et al. to read on a flowable composition. Chow et al. disclose that various additives can be included into the composition including osteoinductive factors (Column 11, lines 51-59 and claim 26). The Examiner interprets an osteoinductive factor to be synonymous with an osteoclastogenic agent. Mixing of the ingredients produces a paste that sets into calcium phosphate containing product (Column 4, lines 39-45) (Instant claims 1 and 15).

Chow et al. do not expressly disclose whether to mix the osteoinductive factor into the dry cement powder or the aqueous setting fluid (instant claims 2, 3, 16 and 17). However, it is prima facie obvious to one of ordinary skill in the art to mix the osteoinductive factor into one or the either or both. See: In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.)

Chow et al. disclose mixing 0.075 mL of aqueous solution with 0.3 grams of calcium phosphate cement powder, which is a ratio of 0.25:1 (Instant claim 10). Chow et

al. disclose cements, slurries and pastes (Abstract; column 1, lines 12-17; column 4, lines 34-38 and column 11, lines 51-52) (Instant claim 11). Chow et al. disclose setting times between about 5 and 10 minutes with specific examples setting in 5, 7 and 8 minutes (See: Column 8, Table II, examples 1-4 and Column 9, Table II example 8 as representative examples) (Instant claims 13 and 21). Chow et al. disclose that the inventive cement can be employed to substitute for missing or defective bone or tooth tissue (hard tissue defects) and can be applied to the site of the defect with a spatula (column 4, lines 34-38 and column 11, lines 18-20) (Instant claim 24). Chow et al. disclose kits of the composition (column 11, lines 12-15) (Instant claim 25).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to include osteoclastogenic agents in the composition of Chow et al. to produce the instant invention. One of ordinary skill in the art would have been motivated to do so because Chow et al. suggests that bone growth regulating agents, i.e., osteoinductive factors and bone morphogenic proteins, can be incorporated into the composition which would aid in the healing process.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teaching of the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Claims 1, 12, 15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al. (US 5,525,148) in view of Constantz (US 6,375,935).

The reference of Chow et al. is described in detail above and that discussion is hereby incorporated by reference.

Chow et al. do not expressly disclose the solution of a soluble silicate as the setting fluid in their methods for making calcium phosphate containing cements.

Constantz discloses methods and compositions where a soluble silicate solution is used as a setting fluid for calcium phosphate cements (Abstract; Column 7, Examples 1-3; and claim 1).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the calcium phosphate cement of Chow et al. by using a soluble silicate as suggested by Constantz and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Constantz disclose that the calcium phosphate cements employing silicate liquids may be mixed very quickly and easily without specialized mixing devices, set rapidly, and are able to obtain higher strengths due to the lower liquids to solids ratios employed (Column 7, lines 54-60).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 1-13, 15-19, 21 and 23-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al. (US 5,525,148) in view of Yasuda et al. (Proc. Natl. Acad. Sci. USA 1998, 95, 3597-3602).

The reference of Chow et al. is described in detail above and that discussion is hereby incorporated by reference.

Chow et al. do not expressly disclose methods of producing a flowable composition comprising an osteoclastogenic agent, which comprises a modulator (ligand) of RANK mediated osteoclastogenesis.

Yasuda et al. disclose that osteoclast differentiation factor is the ligand mediating the signal to osteoclast progenitors for their differentiation into osteoclasts and it is identical to RANKL (RANK ligand) (Abstract and page 3601, Figure 5, for example). Therefore, Yasuda et al. teach that ligands for RANK can serve as osteoinductive factors.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the composition of Chow et al. with a ligand for RANK for the purpose of modulating osteoclast cells to produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Chow et al. suggest that bone growth regulating agents, i.e., osteoinductive factors and bone morphogenic proteins, can be incorporated into the composition which would aid in the healing process. The adjustment of particular working conditions (i.e., the choice of RANK ligand: mimetic, polypeptide, binding fragment, small molecule, etc...) is deemed merely a matter of judicious selection and routine optimization of standard working conditions, which is well within the purview of one of ordinary skill in the art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 1, 14, 15, and 22 rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al. (US 5,525,148) in view of Chow et al. (J. Biomed. Mater. Res. (Appl Biomater) 2000, 53, 511-517).

The reference of Chow et al. is described in detail above and that discussion is hereby incorporated by reference.

Instant claims 14 and 22 recite a limitation wherein the calcium phosphate containing product has a compressive strength ranging from about 25 to 100 MPa.

Chow et al. disclose the measurement of the diametral tensile strength of their calcium phosphate containing cements but do not expressly disclose measurement of the compressive strength (Column 8, lines 12-21 and column 9, Table II).

Chow et al. teach the measurement of both the diametral tensile strength and compressive strength of calcium phosphate cements under a variety of conditions (entire disclosure). The compressive strengths listed in the Chow et al. disclosure are within the range of the instant limitation. Chow et al. note that strengths of the cements are expected to vary with the conditions under which the cement is used (Page 516, last paragraph). Since the composition of Chow et al. (US 5,525,148) appears to be same as the claimed invention then it would intrinsically have a compressive strength within the instantly claimed limitations because a composition and it's properties are inseparable. In addition, the Office is not equipped with the scientific equipment to test the composition of Chow et al. for it's compressive strength. So, when the compositions appear to be the same and the Examiner cannot determine ascertain a specific physical property of the composition in question then the burden appropriately falls upon the Applicant to demonstrate the difference.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to measure the compressive strength of the calcium phosphate containing composition of Chow et al.

One of ordinary skill in the art would have been motivated to do this because the compressive strength is value needed to determine if the cement has adequate strength for specific clinical applications (Chow et al., page 516, last paragraph).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Claim Rejections - 35 USC § 103

Claims 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chow et al. (US 5,525,148) in view of Constantz (US 6,375,935).

The references of Chow et al. and Constantz are described in detail above and that discussion is hereby incorporated by reference.

At the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art that the kit disclosed by Chow et al. makes obvious a packaged calcium phosphate cement of instant claim 26. Chow et al. disclose that the

cement maybe supplied to the user as a powder which is later mixed with a liquid diluent thus making obvious the separation of the powder from the liquid (Column 11, lines 3-7). The type of "removable barrier" on the packaged cement is deemed merely a matter of judicious selection, which is well within the purview of one of ordinary skill in the art.

Chow et al. do not expressly disclose adding a soluble silicate to the composition as described above.

Constantz discloses methods and compositions where a soluble silicate solution is used as a setting fluid for calcium phosphate cements (Abstract; Column 7, Examples 1-3; and claim 1).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the calcium phosphate cement kit of Chow et al. by using a soluble silicate as suggested by Constantz and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Constantz disclose that the calcium phosphate cements employing silicate liquids may be mixed very quickly and easily without specialized mixing devices, set rapidly, and are able to obtain higher strengths due to the lower liquids to solids ratios employed (Column 7, lines 54-60).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because

every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

I. Claims 1, 11, 12, 15, 24, and 25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, 11, 22 and 23 of copending Application No. 10/900,029 in view of Chow et al. (US 5,525,148). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1, 15, and 23-25 are generic to all that is recited in claims 1, 22 and 23 of the copending application. Both sets of claims are drawn to a method of producing a flowable composition that sets into a calcium

phosphate containing product, said method comprising: combining a setting fluid (a solution of a soluble silicate) and a dry reactant component comprising a calcium and/or phosphate reactant wherein the flowable composition is a paste. Instant claim 11 and copending claim 9 are drawn to a paste. Instant claim 12 and copending claim 11 are drawn to a soluble silicate setting fluid. Instant claims 1 and 15 and copending claim 1 are drawn to a method of producing a flowable composition/paste that sets into a calcium phosphate containing product. Claim 24 of the instant invention and claim 22 of the copending application are drawn to a method of repairing a hard tissue defect. Instant claim 25 and copending claim 23 are drawn to a kit.

One of ordinary skill in the art would have recognized the obvious variation of adding an osteoclastogenic agent to the composition of the instant application. One of ordinary skill in the art would have been motivated to do so because Chow et al. disclose that osteoinductive factors can be included in such compositions (Column 12, line 28). Chow et al. further provide guidance on particle sizes and utilize a range calcium phosphate particles sizes some of which are less than 8 microns (Column 8, Table 1). The adjustment of particular working conditions (i.e., selecting a narrow particle size distribution) is deemed merely a matter of routine optimization, which is well within the purview of one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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